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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/747,963	12/30/2003	Alain Martin	CSI 1.0-007CIP	9919

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EXAMINER	
WEDDINGTON, KEVIN E	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 04/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/747,963	MARTIN, ALAIN	
	Examiner	Art Unit	
	Kevin E. Weddington	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *30-51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Claims 30-51 are presented for examination.

Applicant's preliminary amendment filed December 30, 2003 has been received and entered.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 30-51 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-29 of U.S. Patent No. 6,689,810 B2. Although the conflicting claims are not identical, they are not patentably distinct from each other because the present application teaches a method for treating a pulmonary disease state in a mammal by protecting indigenous in vivo levels of nitric oxide in mammalian cells during ozone inhalation comprising contacting the mammalian cells with a therapeutically effective amount of a nitric oxide mediator,

wherein the nitric oxide mediator is selected from the group consisting of pyruvates, pyruvate precursors, α-keto acids having four or more carbons atoms, precursors of α-keto acids having four or more carbon atoms, and the salts thereof; and the patented application teaches a method for treating a pulmonary disease state in mammals by altering indigenous in vivo level of nitric oxide in mammalian cells comprising contacting the mammalian cells with a therapeutically effective amount of a nitric oxide mediator, wherein the nitric oxide mediator is selected from the group consisting of pyruvates, pyruvate precursors, α-keto acids having four or more carbons atoms, precursors of α-keto acids having four or more carbon atoms, and the salts thereof.

Note column 6, lines 18-20 of the 6,689,810 teaches the nitric oxide mediator is inhaled too. Clearly, by "altering" indigenous in vivo levels of nitric oxide with the active ingredients is the same as "protecting" since nitric oxide mediators are known to "protect" nitric oxide (see column 6, lines 33-36).

Claims 30-51 are not allowed.

Claims 30-32 and 35-51 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-25 of U.S. Patent No. 6,623,723 B2. Although the conflicting claims are not identical, they are not patentably distinct from each other because the present application teaches a method for treating a pulmonary disease stated in a mammal by protecting indigenous in vivo levels of nitric oxide in mammalian cells during ozone inhalation comprising contacting the mammalian cells with a therapeutically effective amount of a nitric

oxide mediator, wherein the nitric oxide mediator is selected from the group consisting of pyruvates, pyruvate precursors, α-keto acids having four or more carbons atoms, precursors of α-keto acids having four or more carbon atoms, and the salts thereof; and the patented application teaches a method for treating bronchial constriction and a method for treating airway diseases with a compound selected from the group consisting of pyruvate and pyruvate precursors that are administered by inhalation. Clearly, the present application's broad "pulmonary disease state" encompasses the patented application's bronchial construction and airway disease".

Claims 30-32 and 35-51 are not allowed.

Claims 30 and 33-51 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-27 of copending Application No. 10/205,354. Although the conflicting claims are not identical, they are not patentably distinct from each other because the present application teaches a method for treating a pulmonary disease stated in a mammal by protecting indigenous in vivo levels of nitric oxide in mammalian cells during ozone inhalation comprising contacting the mammalian cells with a therapeutically effective amount of a nitric oxide mediator, wherein the nitric oxide mediator is selected from the group consisting of pyruvates, pyruvate precursors, α-keto acids having four or more carbons atoms, precursors of α-keto acids having four or more carbon atoms, and the salts thereof; and the copending teaches a method for treating bronchial constriction and a method for treating airway diseases with an alpha-keto acid selected from the group consisting of oxaloacetic acid, keto—glutaric acid, keto-

butyric acid, keto-adipic acid, keto-caproic acid, keto-isovaleric acid, their salts and mixtures thereof that are administered by inhalation. Clearly, the present application's broad "pulmonary disease state" encompasses the copending application's bronchial construction and airway disease".

Claims 30 and 33-51 are not allowed.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 30-32, 35 and 43-51 are rejected under 35 U.S.C. 102(b) as being anticipated by Katz (WO 97/10818), Katz (5,798,388; 5,939,459; and 5,952,384).

The four Katz references, each individually, teach methods and compositions for treating a disease state in a mammal caused by inflammatory response. The references teach the disease state is treated with an inflammatory mediator (nitric oxide mediator). Note the inflammatory mediator is at least one compound selected from the group consisting on a pyruvate or a pyruvate precursor. Note the pyruvate are the same as the applicant's preferred pyruvates and the pyruvate precursors are the same also. Note the references disclose the disease state treated in an airway

disease, such as emphysema, cystic fibrosis, acute bronchiectasis, and asthma, all encompassed by the applicant's pulmonary disease state of claim 30. The references teach the inflammatory mediator (nitric oxide mediator) may be administered prior to, after and/or with other therapeutic agents. The additional therapeutic agents are antibacterials, antivirals, antifungals, antihistamines, proteins, enzymes, hormones, nonsteroidal anti-inflammatories, cytokines and steroids. The references teach the inflammatory mediator (nitric oxide mediator) can be administered prior to, concomitantly, and after administration of the inflammatory mediator. Most importantly, the inflammatory mediator (nitric oxide mediator) along or in combination with other therapeutic agent is administered by inhalation. Clearly, the four cited references anticipate the applicant' instant invention; therefore, the instant invention is unpatentable.

Claims 30-32, 35 and 43-51 are not allowed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 30 and 33-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fink et al. (WO 02/074301 A1) in view of Radhakrishnan et al. (5,192,528).

Fink et al. teach the use of alpha-ketoalkanoic acid or their physiologically acceptable salts for example C3-C8 alpha ketoalkanoic acids such as alpha-ketobutyric acid, alpha-ketopentanoic acid, and alpha-ketohexanoic acid, for the treatment of cytokine-mediated inflammatory conditions including asthma.

The instant invention differs from the cited reference in that the cited reference does not teach the addition of therapeutic agents. However, the secondary reference, Radhakrishnan et al., teaches the use of corticosteroid for the treatment of asthma, wherein in said corticosteroid is delivered by inhalation (see abstract and claims). However, one skilled the art would have assumed the combination of two individual agents well-known to treat asthma into a single composition would get the additive effect in the absence of evidence to the contrary.

The instant invention differs from the cited references in that the cited references do not teach the Fink et al. can be administered by inhalation and the specific dosage amounts. However, one skill in the art would have been readily optimized effective dosage and concurrent administration dosage forms as determined by good medical practice and the clinical condition of the individual patient. Regardless of the manner of administration, the specific dose may be calculated according to body weight, body surface area or organ size. Further refinement of the calculations necessary to determine the appropriate dosage for treatment involving each of the above mentioned formulation is routinely made by those of skilled in the art and is within the ability of tasks routinely performed by them without undue experimentation. One would have been motivated to combine

these references and make the modification because they are drawn to same technical fields (constituted with same ingredients and share common utilities) and pertinent to the problem with applicant concerns about.

Claims 30 and 33-51 are not allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kevin E. Weddington whose telephone number is (571)272-0587. The examiner can normally be reached on 11:00 am-7:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571)272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Kevin E. Weddington
Primary Examiner
Art Unit 1614

K. Weddington
April 3, 2006